Vol. 67, No. 3 Established 1884 March 1950

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JOHN FITCH LANDON, M.D., Editor

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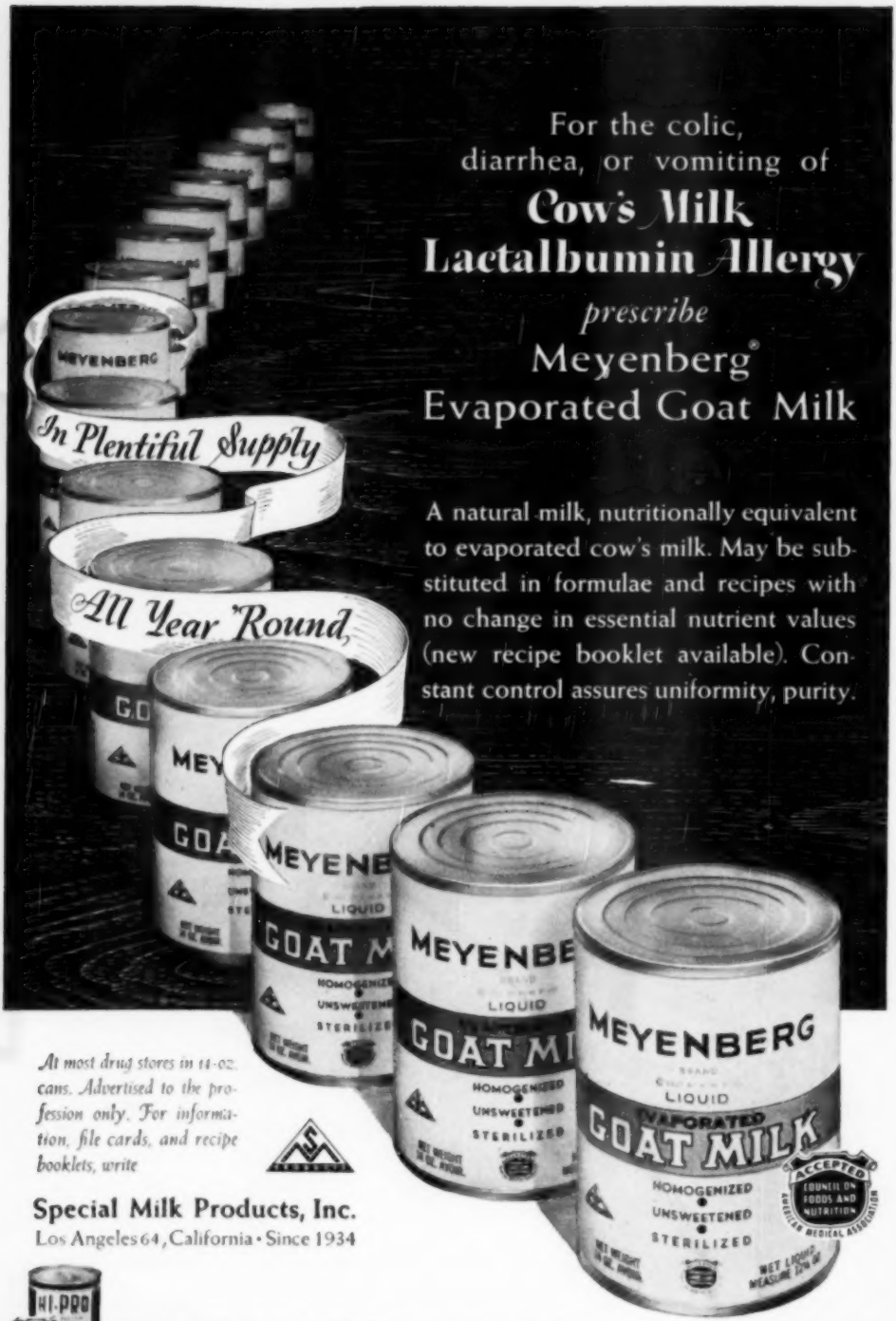
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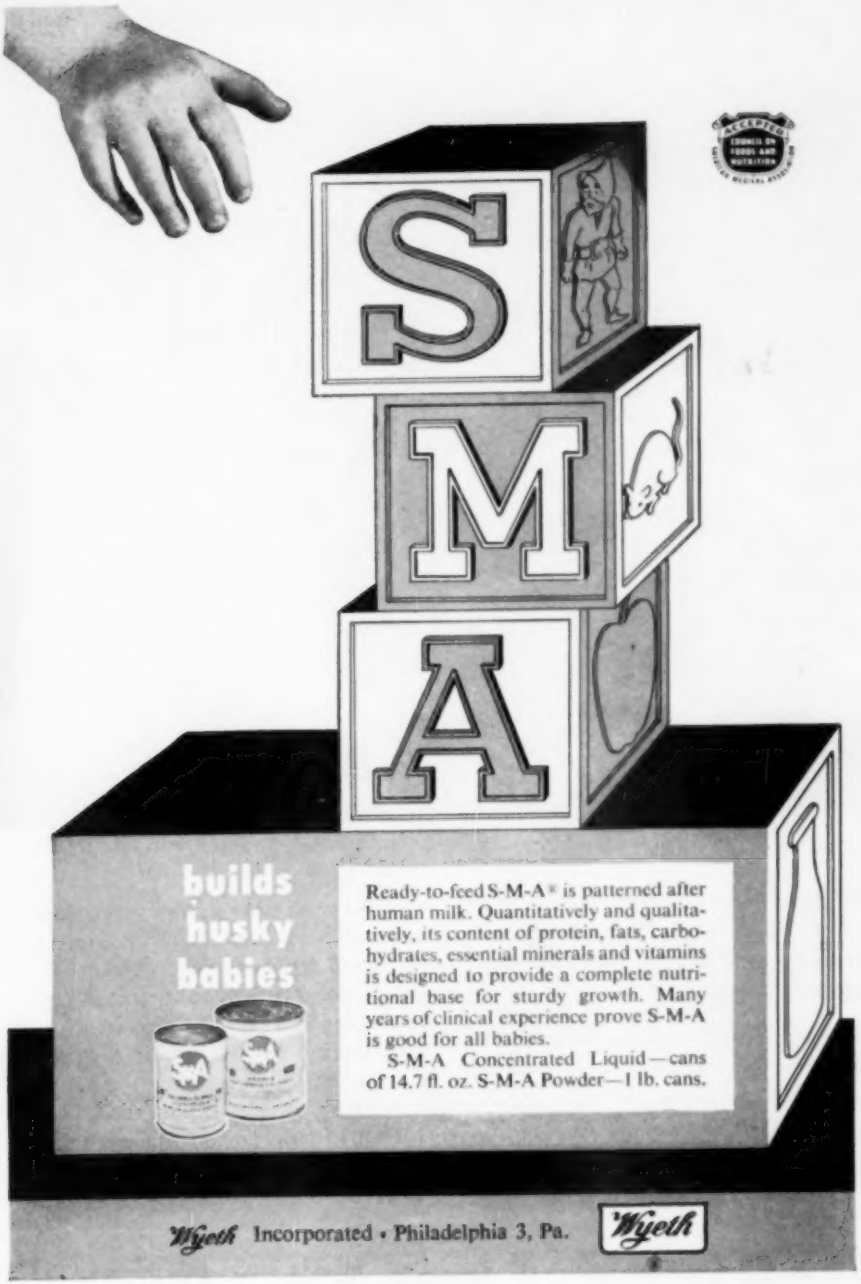
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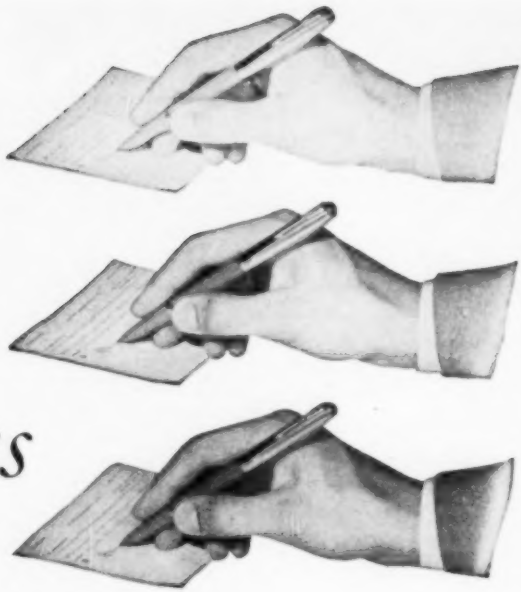

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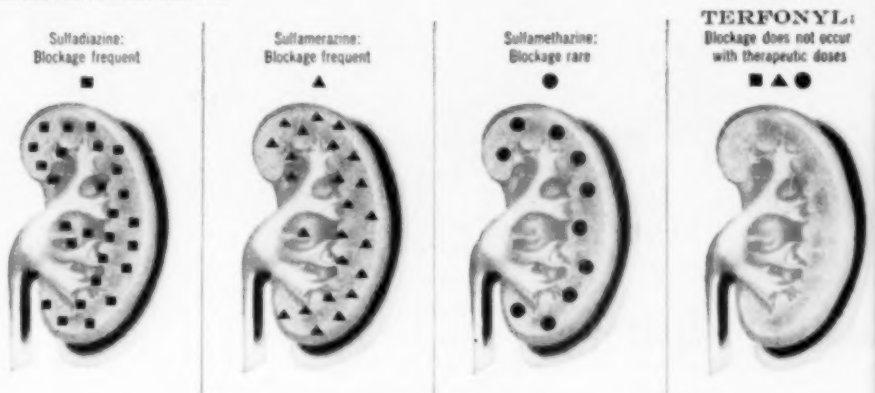

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SEPTICEMIA IN INFANCY*

INCIDENCE OF ASSOCIATED CONGENITAL ANOMALIES

JOHN J. KANGOS, M.D.
New York.

Much has been written concerning the etiology, diagnosis and treatment of sepsis in infancy. In assembling a series of cases of sepsis in infancy the author was impressed with the rather definite incidence of developmental anomalies. The literature was carefully reviewed but no mention of any such relationship could be found. This study was therefore undertaken to demonstrate this observation. In reviewing the case reports of Dunham[1] and Silverman and Homan[4], a similar incidence of anomalies was found. An analysis of the latter series is compared with this study.

PRESENT STUDY

Eleven cases of sepsis in infancy taken from admissions to the Metropolitan and Flower and Fifth Avenue Hospitals of New York City over the eleven-year period from 1938 through 1948 inclusive have been reviewed (see Table 1). The cases in this series include only those with positive ante mortem blood cultures or those diagnosed as sepsis at post mortem examination. Cases with obvious primary foci of infection have not been included.

Three cases were proven with ante mortem blood cultures and in eight cases the diagnosis was made on post mortem examination.

*From the Department of Graduate Pediatrics, New York Medical College Flower and Fifth Avenue Hospitals.

Even though this span includes the period of chemotherapeutic and antibiotic therapy with penicillin and streptomycin of late, the mortality rate remains high with nine (81.8 per cent) deaths noted. Five (45.5 per cent) of the cases studied are within the newborn period. The oldest patient was fifteen months of age. There were six males and five females.

TABLE 1. *Review of Cases*

Case No.	Age	Sex	Ante Mortem Blood Culture Positive	Developmental Anomaly	Post Mortem Diagnosis of Sepsis
1.....	1 day	Male	+	—	Pt. recovered
2.....	7½ mos.	Female	—	—	+
3.....	13 days	Male	—	+	+
4.....	15 mos.	Female	—	+	+
5.....	10 mos.	Female	+	—	Pt. recovered
6.....	6 mos.	Male	—	+	+
7.....	1 day	Male	+	+	Autopsy not obtained
8.....	1 day	Female	—	—	+
9.....	4 mos.	Male	—	—	+
10.....	3 wks.	Female	—	—	+
11.....	5 wks.	Male	—	—	+

\+ Symbol for "present."
— Symbol for "absent."

Eight post mortem examinations were made. Congenital anomalies were found in three (37.5 per cent). In case No. 7, a fatality, there was a strong clinical impression of the presence of congenital heart disease with superimposed subacute bacterial endocarditis. However, since no autopsy was obtained, this case is not included in the percentage figures.

REVIEW OF THE LITERATURE

The largest series reported in the literature include those of Dunham[1] with 39 cases, Chiappa[2] with 51 cases, Todd[3] with 15 cases and Silverman and Homan [4] with 25 cases.

In 1933 Dunham reported 39 cases of sepsis of the newborn. Thirty occurred in boys and nine in girls. Thirty cases were proven with blood cultures ante mortem and nine with post mortem examinations. In this prechemotherapeutic experience a high mortality of 34 deaths (87.2 per cent) was noted. Symptoms appeared during the first two weeks of life in 28 of 39 cases. Twenty

post mortem examinations were made. In reviewing the reported post mortem diagnoses seven (35 per cent) of the twenty cases were found to have developmental anomalies. Four of the seven were in male newborns, two of which included anomalies in the genito-urinary tract.

The 25 cases of sepsis in the newborn reported by Silverman and Homan[4] had one or more positive ante mortem blood cultures each. Nineteen of the 25 cases were males. Fourteen infants died and 11 complete autopsies were performed. Congenital anomalies of major significance with late onset of septicemia were omitted. Nevertheless, congenital anomalies were found in three (27.2 per cent) of the 11 post mortem examinations reported.

85.4 per cent of the cases of Chiappa[2] were newborns. Twenty-six were males and 25 were females. The incidence of congenital anomalies in this series and in the series of Todd[3] have not been reviewed.

The following anomalies were found in the above reviewed series: stenosis of the ureters, congenital unbilical hernia, patent urachus, patent foramen ovale, bilateral double ureters, bilateral hydro-ureters, supernumerary toes, patent ductus arteriosus, suprarenal rests in testes, cleft palate, congenital cysts of kidneys, congenital contracture of bladder neck, congenital bilateral hydronephrosis and microcephaly. It is altogether possible that a closer examination of the above series, including cases which recovered and those which did not go to autopsy, would reveal a somewhat larger incidence of anomalies.

COMMENTS

It is not within the scope of this paper to discuss the frequency of various physical findings or type of offending organism. Onset of symptoms is usually sudden. Physical examination reveals these infants to be ill, but the focus of infection or the portal of entry is either hidden or suspected portals show minimal if any evidence of infection.

Sepsis should be suspected in any infant with a combination of fever, jaundice[4] and inexplicable loss of weight[5,6]. The most important condition to be ruled out in the newborn is erythroblastosis fetalis. A rather constant frequency of congenital anomalies associated with cases of proven sepsis in infancy has been demon-

strated. Five of the cases in this series were within the newborn period. Where erythroblastosis fetalis has been ruled out, therefore, the possibility of the presence of some congenital anomaly should be considered.

The presence of an anomaly in a given case of sepsis, however, may or may not be contributory to the patient's acute illness. In no instance, except for Case 7 in the present study have the congenital anomalies served as an obvious factor in bringing about or perpetuating the septicemia. The significance of anomalies, such as accessory spleens or clubbed foot in this series, and those of cleft palate and supernumerary toes and suprarenal rests in testes, cannot be evaluated at this time.

The newborn is peculiarly vulnerable to infections for several reasons. First, there are unusually favorable portals for entrance of pathogenic bacteria.[2,7,8,9,10] Second, the newborn possesses little resistance to pyogenic bacteria either by passive transfer of antibodies, the ability to manufacture specific antibodies,[7] or possibly owing to deficient leukocytosis or defective development of lymphatic apparatus.[9] The occurrence of anomalies in some of these cases is in itself indicative of the presence of stunted developmental processes in these infants. Perhaps there is a concomitant maldevelopment or immaturity of some anatomic structure whose function is vital in warding off or combating infectious processes. The findings in this study, therefore, may be interpreted as further evidence explaining the peculiar vulnerability of infants, particularly newborns, to infection.

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ASPHYXIA, TRAUMA AND SHOCK AT BIRTH*

PETER GRUENWALD, M.D.
Brooklyn.

In the course of the pathologic examination of a large number of newborn infants at autopsy, a high incidence of the well-known manifestations of mechanical birth trauma and asphyxia was found. In addition, other lesions, which had previously not been recognized, were encountered; analysis of the circumstances under which they occurred revealed that they predominate in infants with clinical and pathologic evidence of asphyxia at birth. Several observations led to the suggestion that the lesions are caused by shock associated with asphyxia. The relationship of these conditions to mechanical trauma was also examined. The result of this investigation is an hypothesis concerning the mutual relations of asphyxia, trauma and shock which incorporates most of the pathologic conditions frequently found in newborn infants. Obviously, this hypothesis will have to be confirmed or modified by observations on living infants in order to evolve into a definitive concept. This hypothesis will now be presented not only in order to invite critical examination by means of clinical research, but also because even in its present form it may be of value to obstetricians and pediatricians in the evaluation of preventive and therapeutic measures.

PATHOLOGIC OBSERVATIONS

The following summary of findings at autopsy includes both the well-known signs of asphyxia, and those additional changes which, in this author's experience, also occur in asphyxiated infants. Only those few aspects of mechanical birth trauma will be discussed in which there is disagreement with current opinion, or a close relationship with other points under consideration.

The observations were made in autopsies on more than 500 infant three days old or younger, including those born dead. After more than three days of extrauterine life many of the

*Presented at a meeting of the Research Society of the Long Island College of Medicine, May 11, 1949.

From the Departments of Pathology, Long Island College of Medicine and Kings County Hospital, Brooklyn.

Publication No. 8 of the Brooklyn Survey of Neonatal Pathology. Many hospitals in Brooklyn have contributed material to this project, which is supported by a research grant from the Division of Research Grants and Fellowships of the National Institutes of Health, U. S. Public Health Service.

immediate effects of paranatal asphyxia have disappeared, so that one can no longer obtain a complete picture of the changes which existed shortly after birth. Severely asphyxiated infants probably do not reach this age. A list of the previously known and the newly suggested pathologic lesions in neonatal asphyxia will be found in Table 1. A statistical evaluation of the incidence of each lesion is now in progress and will be reported at a later date.

TABLE 1. *Pathologic Changes Found in Asphyxiated Infants*

	Previously Known Changes	New Findings
General	Yellow vernix caseosa* Focal hemorrhages Venous congestion	Edema*
Heart		Myocardial damage (fatty change, dilatation) Necrosis in arteries
Lungs	Aspiration of amniotic sac contents* Hyaline membranes	Edema with secondary pneumonia
Liver	Cytoplasmic degeneration	Degeneration predominant in right half* Focal necrosis Necrosis in arteries
Pancreas		Inflammation Hemorrhagic necrosis
Adrenal cortex		Congestion, hemorrhage Focal necrosis
Digestive tract		Ulcerative esophagitis Gastric erosions Focal hemorrhagic necrosis
Brain	Focal hemorrhages Degeneration with cyst formation	Subarachnoid hemorrhage

* These changes are particularly suggestive of prenatal anoxia even when found in liveborn infants.

Known Lesions in Asphyxia. The following well-known signs of asphyxia are often found in newborn infants. The surface of the body may be covered with golden yellow vernix caseosa, owing to previous discharge of meconium into the amniotic cavity under

the stimulus of anoxia.[1] Further inspection of the body and its cavities may reveal severe congestion of blood vessels and petechial hemorrhages in the skin, serous and mucous surfaces, and the parenchyma of organs. Scattered small hemorrhages in the brain are found in severe cases. Extensive degenerative changes with cyst formation have been found in the brain of severely defective older children, and there are indications that some of them are due to paranatal anoxia.[2]

The lungs show not only congestion and hemorrhages, but also the effects of respiratory movements stimulated by anoxia. The alveoli may be filled with large amounts of vernix caseosa or meconium, and in some of these instances there is pneumonia. Hyaline membranes in bronchioles, believed by some investigators[3] to consist of aspirated fatty vernix, are probably caused by intrauterine asphyxia and subsequent air breathing. They are invariably associated with extensive atelectasis and lead to aggravation of anoxia after birth.

Changes in the liver cells, including various forms of cytoplasmic degeneration, are common in the infants under consideration. Gillman and Gillman[4] have found them to be identical with those in adults who died of asphyxia.

New Observations. In addition to lesions just described, a variety of others have been found to occur, particularly in those infants who had the above mentioned signs of asphyxia to a severe degree, and often also a history of long or otherwise complicated labor, or difficult resuscitation.

Edema and effusions in serous cavities are often conspicuous. An interpretation of their significance will be given later. The heart may show dilatation of its chambers and a flabby myocardium. Microscopically, the myocardial fibers may contain considerable amounts of stainable fat. Arteries in the epicardium and myocardium show degeneration and hemorrhage in their adventitia, and occasionally focal necrosis in the media; this has been described in detail elsewhere.[5]

The pulmonary alveoli often contain much fluid. In infants who died at birth or shortly afterward, this may be wholly or in part amniotic fluid. If more than a few hours have elapsed since birth, this explanation is no longer acceptable since fluid can be rapidly absorbed from the lungs. In these instances fluid in the alveoli

represents edema, unless other findings suggest an inflammatory exudate. In cases in which the diagnosis of pneumonia is made, there are often just a few scattered leukocytes; bacteria are not always found, and when they are present, they are of various types. The occurrence of aspirated amniotic sac contents was mentioned above.

In the liver, various forms of cytoplasmic degeneration may be found, as was mentioned above. In severe cases there may be multiple foci of necrosis. In some instances these changes are more severe in the right half of the liver than in the left, and that may be conspicuous at autopsy. This lateral difference is due to a peculiarity of the fetal circulation; a supply of arterial blood from the umbilical vein reaches only the tissue of the left half of the organ and appears to have a protective action so that this half is less affected by anoxia.[6] Necrosis in the media of arteries occurs in some instances; it resembles changes that occur in the heart.

In a few asphyxiated stillborn or newborn infants the pancreas was the seat of scattered areas of dense infiltration with polymorphonuclear leukocytes; in one instance with very severe signs of asphyxia there was complete hemorrhagic necrosis.

The adrenals are often severely congested in their central portions; in severe cases the tissue between the capillaries shows various degrees of damage and destruction, so that transitional states may be found between congestion and focal or massive hemorrhage. In none of these cases was a laceration found; the central portion of the cortex was always most severely affected. The relationship of these findings of hemorrhage to mechanical birth trauma will be discussed later. Other asphyxiated infants show areas of necrosis in the cortex with disintegration of cells. The location is uniformly in the inner portion of the permanent cortex, and occasionally a continuous zone is similarly affected. It is conceivable that necrosis may enhance the transition from a state of congestion to massive hemorrhage. The adrenal medulla is poorly differentiated at birth, and no characteristic lesion has been found in it.

No significant and conspicuous lesion has so far been discovered in the kidneys. Severe venous congestion and focal hemorrhage are frequent. The internal genitalia are also subject to severe congestion. This is most prominent in the vessels near the hilus of the testis. In this location and in the testis itself hemorrhage

may occur, varying from small foci to large areas. This has long been known to occur in newborn infants. It is my impression that asphyxiated infants are particularly affected, and that this is part of the widespread congestion and tendency toward hemorrhage. The ovary may be the seat of lesser degrees of congestion. In the uterus the vessels of the endometrium or the subserous tissue may be strikingly engorged. Hemorrhage in the tissue of the endometrium rarely occurs.

In the gastro-intestinal tract lesions of the esophagus are the commonest. They range from severe hyperemia through various intermediate forms to extensive ulcerations which may give rise to hemorrhage or, in rare cases, perforate into a pleural cavity.[7] Ulcers do not begin to develop until several hours after birth. In some instances the lesions contain various types of microorganisms which are presumably secondary invaders. This ulcerative esophagitis never extends to the stomach, but gastric erosions occur. In other cases the stomach or duodenum contains small areas in which the mucosa is intensely congested, and there is extravasation of blood and necrosis of some of the tissue. More distal parts of the intestine have not revealed any lesions.

No infant has been examined in whom all of the lesions described were present; however, several instances are on record in which many of the changes existed.

DISCUSSION

Evidence of Shock. When the association of the new pathologic findings with asphyxia was first recognized, it was not clear how some of them could be accounted for. A satisfactory concept evolved only when it was suggested that asphyxiated infants may be in shock, and that some of their pathologic features are shock lesions. In discussing this subject, it would be convenient to have on hand an authoritative and generally accepted description of all pathologic lesions occurring in shock. This, however, is not available because of the controversial state of our knowledge. The present discussion follows Moon's[8] presentation of the subject, and that part of Seyle's[9] summary of the pathologic changes in the general adaptation syndrome which deals with acute lesions presumably originating during the "shock phase of the alarm reaction." Regarding the gastro-intestinal manifestations, human and experi-

mental pathology of shock, as described by Penner and Bernheim,[10] will be used for comparison.

Another reason why it is difficult to determine just which of the changes enumerated in Table 1 are indicative of shock, is that shock and anoxia are so intimately related to one another that some of their manifestations cannot be separated. Moon[8] has explained in detail the mutual relations of the two conditions, and the manner in which they join in a vicious circle.

Edema and focal hemorrhages are indicative of increased capillary permeability which, according to Moon,[8] is one of the fundamental factors in shock. Of particular interest is the relatively severe edema of some newborn infants. Its origin is explained by the peculiar environment of the fetus. In an independently living individual, abnormal permeability of capillaries due to asphyxia and shock causes the diffusion of a limited amount of fluid from the blood into the tissue spaces. In the fetus, however, the placenta supplied by maternal blood furnishes a practically unlimited reservoir of fluid which may be taken up into the fetal blood stream to compensate for the loss to the tissues. Thus more fluid is available which may in turn leave the vessels and accumulate in the fetal tissues. Recent experiments with guinea pig fetuses in utero with Moon's[8] standard method for the production of shock in animals (intraperitoneal administration of muscle pulp) have resulted in severe edema of the fetus, and thus support the hypothesis that edema or, in severe cases, hydrops may be a manifestation of shock in utero.[11]

The type of pneumonia described above, in which there is much fluid in the alveoli with relatively few leukocytes and an inconstant bacterial flora, corresponds exactly to that described by Moon[8] in shock as a secondary change in edematous lungs. It is known that irritation by aspirated amniotic sac contents alone does not cause pneumonia; one frequently finds these substances in the lungs of infants several days of age, without any inflammatory reaction.

Cytoplasmic degeneration in the liver, with focal necrosis in some cases, is known to occur not only in anoxia, but also in the alarm reaction (part of which corresponds to shock) due to other causes.[9]

Inflammation and necrosis in the pancreas were at first included among the changes in asphyxia solely on the basis of their occur-

rence together with other lesions under consideration. The association with asphyxia could be explained only on the basis of Seyle's experience, according to which similar pancreatic lesions may develop in the course of the alarm reaction.[12]

On a similar basis, the occurrence of necrosis and hemorrhage in the adrenals is readily explained. The adrenals are known to react prominently during the alarm reaction, often in a similar manner as was described above.[9] Hemorrhage in some of the present cases resembles that in the Waterhouse-Friedrichsen syndrome where it has been interpreted as a manifestation of the alarm reaction by Seyle.[9] The appearance of hemorrhage in infants' adrenals does not suggest mechanical trauma as a cause.

Perhaps the most suggestive findings as far as shock is concerned are those in the digestive tract. Esophagitis, as well as areas of hemorrhagic destruction of the mucosa, correspond in every detail to observations of Penner and Bernheim[10] in shock of human subjects and experimental animals. No other explanation of these lesions in infants has been found.

In view of these considerations, it appears fair to assume that many asphyxiated newborn infants are in shock. If one follows Moon's[8] concept, this might be postulated on theoretical grounds as well. In view of the above mentioned close relations of the two conditions involved, no attempt will be made to separate clearly all lesions directly due to asphyxia from those caused by shock.

Mechanical Birth Trauma. It remains to discuss briefly the manner in which mechanical trauma is related to asphyxia and shock. It is generally known that mechanical brain damage, involving the respiratory centers, may cause asphyxia after birth. The possibility of shock being caused by mechanical trauma, with or without extensive morphologic lesions, is also obvious. However, the predisposition to mechanical trauma existing in a state of asphyxia is not generally appreciated. Few investigators[13] have noted that severe venous congestion in asphyxia renders the liver more susceptible to trauma. The highly vulnerable state of a congested liver is obvious at autopsy when, in spite of careful handling, hematomas and lacerations often arise under the pathologist's hands. It is also fair to assume that the brain and its meninges will more readily give rise to serious hemorrhage when their blood vessels are extremely engorged as happens in asphyxia. To what

extent parenchymal damage in the liver or brain increases the susceptibility to trauma cannot be reliably estimated.

There are doubtless instances in which hemorrhage due to anoxia has been mistaken for mechanical trauma at autopsy. This may occur in the cerebral arachnoid when focal hemorrhages are large and confluent. Such hemorrhages of considerable size have been seen in infants delivered by Cesarean section. Smaller hemorrhages scattered elsewhere in the arachnoid may help establish the diagnosis of asphyxial lesions.

Hemorrhage in the adrenals has repeatedly been classified as an instance of mechanical birth trauma.[14] It was mentioned above that transitional states exist between outright hemorrhage and severe venous congestion which is common in asphyxia. Hemorrhage is typically located in the central portion of the cortex, and as a rule no lacerations are found. For these reasons it is suggested that adrenal hemorrhage in the newborn is usually not due to mechanical trauma, but rather to asphyxia and shock associated with it.

Incidence of Lesions. When reviewing autopsy findings in newborn infants, one is impressed by the very high incidence of signs of asphyxia and shock. Infants born at or near term generally show these signs in greater variety and severity than small premature ones; no satisfactory explanation of this observation has been given. It may be that premature infants tend to be less asphyxiated owing to a relatively greater oxygen reserve in their maternal blood supply,[15] or to shorter labor, or else the same degree of asphyxia may produce less conspicuous morphologic alterations. The latter possibility must be viewed with reservation since the capillaries of premature infants are known to be less resistant than those of infants born at term.[16] Among mature infants it is difficult to find at autopsy even a few who do not have several of the above mentioned changes. This indicates that most of them have gone through a period of severe anoxia which may or may not be secondary to some other abnormal condition within the infant.

In making this statement, it is realized that the same might be true in the last analysis of almost every death. Yet, the signs which are so common in these infants are rarely seen in older children or adults, except in cases of outright suffocation or similar accidents. There appears to exist either a fundamental, or a

marked quantitative difference between the circumstances under which death occurs in most newborns on the one hand, and older persons on the other hand. It is known that newborn infants are more resistant to anoxia than adults as far as length of survival is concerned.[17] Perhaps this gives newborn infants time to develop severe lesions whereas older individuals would have died sooner, before acquiring these morphologic changes.

Among full-term infants who die within three days after birth the incidence of mechanical trauma is much lower than that of asphyxia. In premature infants there is a higher occurrence of trauma and a lower incidence of morphologic signs of asphyxia. A statistical evaluation of related autopsy findings will be reported at a later date. The following data, taken from a study of liver lesions,[6] may be taken as an indication of the cumulation of lesions in a group of asphyxiated infants. Among 38 infants with degeneration of the liver predominant in the right lobe which indicates intrauterine anoxia (see above), there were 5 who also had all of the following lesions: aspiration of vernix caseosa, petechial hemorrhages, necrosis in the wall of coronary or hepatic arteries, and esophagitis or gastric erosions. Among 16 liveborn infants dying during the first three days and showing the above mentioned type of degeneration in the liver, 12 also had esophagitis or gastric erosions.

Relationship of Asphyxia, Trauma and Shock. The preceding considerations suggest a concept of the mutual relations of asphyxia, trauma and shock which is summarized in a diagram in Fig. 1. In surveying the effects of these three conditions on newborn infants it is considered more important and useful to stress their close relationship rather than attempt a clear-cut separation or pathologic differential diagnosis in all instances.

In view of the very close functional relation of asphyxia and shock which has been discussed and illustrated by diagrams by Moon,[8] it is hardly conceivable that one of the two could reach any degree of severity without producing the other. In combination, the two produce a variety of lesions in the viscera which were described above. How many of these visceral lesions are terminal, or occur only in the irreversible late phase of shock, is not known.

There is also a mutual relation between asphyxia and mechanical trauma. It has been known and appreciated for a long time

that injury of the respiratory center or other vital parts of the central nervous system is responsible for some instances of asphyxia. Somewhat less appreciated is the increased susceptibility of asphyxiated infants to mechanical trauma; this is due to severe venous congestion and perhaps parenchymal damage of various organs.

It is obvious that mechanical birth trauma, just like any other injury, may lead to shock. Largely of pathologic interest is the

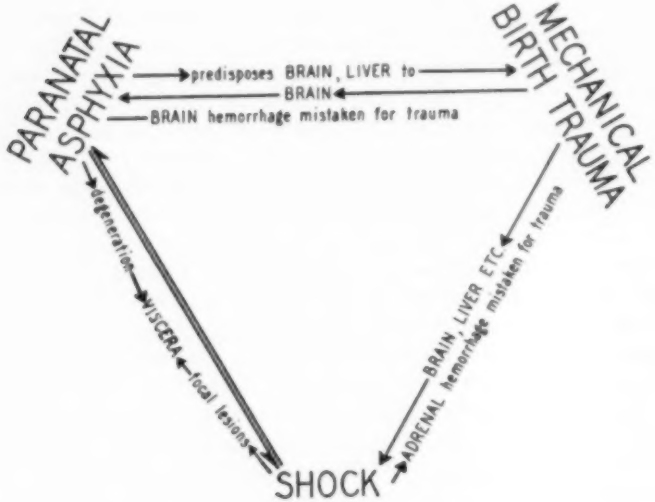

Fig. 1. Diagram of the mutual relations of asphyxia, trauma and shock in newborn infants.

suggestion that asphyxia and shock may produce hemorrhage which has been mistaken for trauma, namely in the adrenals and in the brain including the meninges.

A variety of causes intrinsic or extrinsic to the fetus may be responsible for the pathologic changes which were dealt with in the preceding pages. These will not be discussed as nothing new could be added to existing knowledge. It would certainly be most desirable to understand and control these causes sufficiently to eliminate them and prevent their effects on the infant. However,

it is probable that no advances will ever completely eliminate asphyxia and trauma at birth.

Suggestions for Treatment. New evaluation of clinical and pathologic findings with the present concept in mind may lead to a better appreciation of the advantages and dangers of various obstetrical procedures and methods of treatment of the infant. On the other hand, the present tentative concept needs to be confirmed by observations on living infants if it is to be definitively accepted. In view of the difficulties in the objective diagnosis of the changes under consideration in living infants, the present hypothesis may be found valid only if treatment based on it is successful. It should be made clear that whatever suggestions for treatment are made are meant to be integrated with methods currently in use, rather than replace the latter.

Therapeutic measures which might be indicated on the basis of the present observations may be divided into two groups: one concerned with the general syndrome of shock, and the other one dealing with lesions in various organs which may require separate attention.

Treatment of shock may have to be undertaken in the absence of signs which are used in the diagnosis of that condition in older persons. Changes in blood pressure, erythrocyte count or body temperature are unreliable in newborn infants. It was mentioned that conspicuous edema at birth, except for that of presenting parts, is suggestive of shock. Hemorrhage from esophageal ulcers occasionally indicates the existence of shock lesions.[7] This sign cannot be expected until some time after birth, as ulcers begin to appear only at about 12 hours of age or later. In the absence of more reliable signs one will have to depend on experience to learn which cases of asphyxia or trauma, or infants who are just in poor condition, may benefit from treatment for shock. In giving fluid intravenously, one should keep in mind that many of these infants are more severely edematous than are older persons in shock. Solutions of readily diffusible electrolytes should therefore be used with the greatest caution, if at all, lest the edema be increased. Blood or its fractions, or colloidal substitutes, appear more suitable, perhaps in such form that they draw fluid from the tissues into the circulation. Smith[15] made a similar suggestion based on the inability of infants' kidneys to excrete electrolytes efficiently.

Among the organs with lesions which may require separate attention are the heart, the liver and the adrenal cortex.

Pathologic evidence of damage to the myocardium and the blood vessels which supply it was mentioned above. Its functional significance should be examined in living infants by cardiologic methods in order to determine whether or not it should be treated. It is possible, however, that the control of shock alone may result in improvement of the condition of the heart, since it is known that the blood supply of the myocardium suffers in shock, and that there is a cumulation of the effects of myocardial damage and shock.[10] The rapid administration of fluid in amounts which are tolerated by other infants may be dangerous in patients with myocardial damage.

Pathologic indications of liver damage should also be supplemented by the use of clinical methods, in order that the desirability of supportive treatment may be established. It would further be worth knowing whether some instances of moderate jaundice shortly after birth are due to anoxia damage of the liver.

There are doubtless instances in which the adrenal cortex is damaged to the extent that this can be demonstrated in autopsy material by crude morphologic methods (see above). In addition there may be many more infants whose adrenal cortex is near exhaustion as the result of shock.[9] It may be worth while to investigate the effect of treatment with cortical hormone not, as has been done, haphazardly in an occasional moribund infant, but systematically and under properly controlled conditions.

In all trials of treatment one should keep in mind that there is in all probability a group of asphyxiated or traumatized infants who are in irreversible shock at the time when treatment can be started; in some instances this may be the case at birth. An attempt should be made to eliminate these cases when the results of therapy are evaluated.

SUMMARY

New evaluation of pathologic findings in autopsies on newborn infants suggests that many of these patients have died in shock. Based on these observations a concept of the mutual relations of asphyxia, trauma and shock at birth is presented, with particular reference to the very close ties between asphyxia and shock.

This concept may be useful in the evaluation of various obstetric and pediatric methods. It is suggested that many newborn infants, who are in poor condition, may require treatment for shock and perhaps also for lesions in various organs, in addition to valuable methods now in use.

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ACUTE LARYNGOTRACHEOBRONCHITIS*

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During the past few years, the medical profession has become increasingly aware of a disease which can be one of the most serious encountered in pediatric practice. It is acute infectious laryngotracheobronchitis, popularly known as "croup." Prior to its pathological and clinical recognition, cases frequently were buried in hospital diagnostic records as bronchitis, laryngitis, pneumonitis, tracheitis or even common cold. In spite of the present awareness of it as an entity, the illness still is too often too lightly regarded. This study was conducted to stress the danger of this prostrating, sometimes fatal disease, and to point out some significant observations concerning it.

There were 332 cases of true laryngotracheobronchitis in this group, combining 293 admitted to the Charles V. Chapin Hospital, Providence, Rhode Island, in the years 1935 to 1948, and 39 taken from the records of the Metropolitan Hospital and the Flower Fifth Avenue Hospitals, New York City, in the years 1943 to 1948. Croup associated with a specific disease, such as diphtheria, and so-called "midnight croup" or "false croup" was excluded.

Definition. The disease may be defined as an acute infection of the larynx, trachea and bronchial tree characterized by inflammation and edema of the larynx, and a thick, tenacious, sticky, purulent secretion which obstructs the lower respiratory passages. One could call this condition a pharyngo-laryngo-tracheo-broncho-bronchiolitis, because in the severe cases, which reach the autopsy table, all these structures are involved.

Pathology. Once the gross pathology has been seen at post-mortem, it can never be forgotten. The larynx is red and inflamed, and if it is removed en masse with the trachea and lungs, one sees the thick, viscid pus oozing out between the vocal cords as the organs are lifted free. The cords are red and edematous. On opening the trachea, the mucosa is found to be swollen and the lumen may be filled for its entire length with ropy, adherent, thick, greenish, purulent matter with the consistency of chewing gum.

*Written as a requirement of the Graduate Course in Clinical Pediatrics, Department of Pediatrics, New York Medical College, Flower and Fifth Avenue Hospital, New York City.

If forceps are used in an attempt to remove some of this material, it will often stretch like a rubber band and break with an audible snap. This condition exists down to the finer ramifications of the respiratory tree. The lungs show scattered patches of atelectasis, and the cut surface is red to purple with consolidation and congestion. If the exterior of the lung is squeezed, fine streams of purulent exudate ooze from the cut surface. The patient was literally drowned in this muck.

Microscopically, the epithelial lining cells of the respiratory mucosa show a loss of cilia. This was pointed out by Lamont[1].

Etiology. This type of croup is a mixed infection in most cases. In this study cultures have shown hemolytic streptococci, staphylococci, pneumococci, influenzal bacilli, and in one case Friedlander's bacillus. Any one of these organisms may be the dominating factor, but it is felt that two or more types of bacteria are usually involved, which accounts for the picture of overwhelming infection and toxicity so often seen. Some cases are of viral origin. Although no virus studies were done in this series, Everhart[2] states that a virus has been isolated and cultured by some observers.

Symptoms. This disease usually has an abrupt onset. It may occur at any time during the day or night. The patient may have had mild upper respiratory symptoms for the preceding 12 to 24 hours, but even this prodrome may go unnoticed. The temperature suddenly becomes elevated, the child may become hoarse, and he develops a croupy cough with an inspiratory crow or stridor noted with each breath. He becomes dyspneic, and there may be extreme prostration and toxemia. There is retraction of the supra- and infra-sternal notches and the intercostal spaces with flaring of the rib margins. The thoracic cage seems to lift and "tug" with each breath. The patient may become cyanotic and develop a moist rattle. There may be some expectoration, but usually the secretion is too thick to be coughed up or the child is too young to have learned how to cough.

As the disease progresses, these patients become dehydrated, prostrated, and finally present a picture of complete collapse. The cyanosis disappears, leaving an ashen pale skin and anoxic coma, with all remaining energy being spent in breathing. Retraction may be so great that the sternum and thoracic spine seem to touch with each gasping inspiration. As Lamont[1] says: "When this

stage is reached there is little hope for recovery. Such a picture is terrifying to the parents and equally so to the doctor."

Physical Signs. Physical examination, which is held to an absolute minimum, shows a general picture such as described. The child may be very excited, frightened, thrashing around and staring wild-eyed in panic. In the extreme cases one will notice the child make swimming motions with its arms as if he were drowning—and that is often exactly what he is doing, drowning in his own secretions.

The pharynx is injected and may be filled with frothy, dry sputum. The chest is full of loud, coarse, inspiratory wheezes and rattles. Moist râles are usually heard, but the inspiratory stridor may be so loud as to obscure breath sounds. In later stages these findings may occur in both phases of respiration. Areas of atelectasis may be present with decreased or absent breath sounds and impaired percussion. Many times there will be fine sticky râles indicating alveolar involvement. The heart rate is rapid and thready, but the quality of tone and presence or absence of murmurs is next to impossible to ascertain because of the loud crowing. One realizes there may be all degrees of this type of croup, but here the severe case is presented to emphasize the potential dangers of the disease.

Observations. The age group is important in prognosis. In the 332 cases of this series, 80 per cent were between 5 months of age and 3 years old, with the highest incidence around 2 years. These findings correlate closely with those of Morgan and Wishart.[2] It is evident this is an affliction of the infant and younger child.

There were 16 deaths and 13 were patients less than 2½ years old. The oldest fatality was 6 years of age, and the youngest 2 weeks. In Lamont's[1] series, 87 per cent of the deaths were in children under 4 years old. The younger the patient the poorer the prognosis.

In this study males outnumbered females in a ratio of 3:1. Morgan and Wishart[2] found 65 per cent males to 35 per cent females in their group, while Davison[4] reports a proportion of 3 males to 1 female.

A striking fact observed in this series has been that a good many of these children were overweight, overfed youngsters with

blooming red cheeks and fat thick extremities—the layman's idea of a healthy child. This has been noted so often that one speaks of the "croup physique." Several predictions made on this basis in a summer well-baby clinic were borne out the following winter when these babies were admitted to the hospital with croup. And these babies are often repeaters, coming in again and again with croup until they have reached an older age group and perhaps run off some excess weight. It is not meant that children of normal weight or even underweight can not have croup, but it is felt that laryngotracheobronchitis has a higher incidence in the overweight group, and when it occurs it usually seems more serious.

The seasonal variation is well-known. This is a cold weather disease with the highest incidence of cases in January and February, and the peak in March. The summer months are relatively free, but an occasional croup is seen. With the approach of fall, the incidence rises. It seemed in this series that quick changes in weather were more significant than continued cold. When there are a few mild days and then a sudden cold snap, the number of admissions to the hospital goes up. It is felt that part of this is due to the sudden increase of heat in the home with the resultant lowering of the humidity. This produces a dry scratchy throat and a ripe field for invading bacteria. Davison[4] suggests that the preceding upper respiratory infection obstructs the nose and causes mouth breathing, the dry indoor air impinging directly on the larynx without being moistened by the nasal passages.

Many homes are still heated with oil stoves and kerosene burners, which after a summer of disuse, emit rank fumes and soot when lighted. This may be responsible for touching off an attack of croup. Frequently, a child will be seen at home in acute distress. Upon arrival at a hospital the parents volunteer the information that the baby seems much better. It is felt that the removal from the arid atmosphere of the home, and the trip through the cold but moist air produce this change. In many cases it is difficult to decide which child should be taken to a hospital and which could be treated at home.

One point which may be helpful in this decision is hoarseness. If the parents think the patient's cry is hoarse or husky, it would be wise to admit that patient. A baby who is "tugging" or re-

tracting should be admitted. If several hours of home treatment do not improve the condition, hospitalization is best. A warning may be in order here concerning the false sense of security which may develop when a child suddenly appears much better after vomiting. This is explained by the removal of bronchial secretion and plugs by the mechanical massage of vomiting. This relief is usually temporary, and the patient is very likely to become worse. Another point is hyperpyrexia. Morgan and Wishart[3] state that a high temperature is a poor prognostic sign. In their series they had 42 cases with a temperature of 106° F. or higher. Death occurred in 37 of them.

Management. The treatment of these patients has always been a precarious problem. The plan of attack is to combat infection, loosen and remove secretions, and to provide supportive measures. The earlier this can be done the better.

These cases should be placed in a humid atmosphere of steam. The disadvantage of this is the high room temperature which usually follows the use of any type of steam room, heater vaporizer or such. However, the benefit of the increased humidity is so important that any method available should be used and the room temperature kept as nearly normal as possible. A type of cold humidifier or air moistener would be best.

Any sign of cyanosis is an indication for oxygen. In this group this was best accomplished by use of an open top tent. Weinstein[5] advocates the use of humidified cool oxygen instead of the usual croup steam tent and suggests that mixtures of helium and oxygen may be more beneficial than straight oxygen. Those children who are restless, excited, or frightened by the oxygen apparatus, should have some sedation.

The amount of sedation is a delicate point of balance which must be weighed in each case. The danger of suppressing the cough reflex and respiratory rate is a real one, but the advantage of quieting the child offsets this by producing more effective respiration. By using small doses of the barbiturates, preferably phenobarbital, sedation can be acquired without too much difficulty. Some observers feel that no sedative should be used, but in this series it has been of great value.

Those children who have frothy or mucoid secretions present in the throat, or who may cough them into the nasopharynx, and

lack the energy to expectorate them, should be suctioned gently with as little disturbance as possible. In some instances, the use of ipecac in emetic doses has been helpful. One should not try to produce more than one or two episodes of vomiting. Logan[4] frequently uses 3-5 drops of saturated potassium iodide solution to help liquefy secretions.

Hydration becomes very important. This can usually be obtained by clysis at first and by mouth in 12 to 24 hours. Nutrition should be maintained.

The most important step in the treatment is the early, vigorous use of the antibiotics. Because this is a mixed infection, any one or more of several organisms may be the etiological factor. Time does not permit the isolation of the offender. The child is too ill. If one were to wait until cultures showed the bacteria present and then started to administer the proper therapeutic agent, many lives would be needlessly lost. Consequently it is felt that the patient should be started on immediate combined therapy of penicillin, streptomycin and aureomycin or chloromycetin. Thus one will combat the gram-positive organisms, the gram-negative bacteria, and any virus which may be present.

The advent of the sulfonamides appreciably reduced the mortality of croup, and the use of these weapons in the form of sulfadiazine or combinations is still good. However, the three antibiotics mentioned will cover practically all the bacteria which might be involved without introducing the added worry of urinary accidents.

Clinically, it takes about 8 hours for a beneficial effect of this therapy to be noted. In the majority of cases, if a child will live for that length of time, adequate blood levels of the antibiotics will be present and the patient will start to improve. This period is the crucial one. It is felt that there will always be a few cases which are so toxic and so overwhelmingly sick and on which treatment is started too late that they will die before these drugs can take effect. This brings up the question of tracheotomy.

It is not hard to see why tracheotomy does not save all cases of acute laryngotracheobronchitis. In some severely toxic children the shock of the procedure is the final blow needed to cause death. In others it is not hard to see why merely by-passing the glottis fails to relieve the pathological picture of obstruction down in the terminal branches of the respiratory tree. To be sure, there

is often dramatic immediate improvement following tracheotomy in some cases. But many times this relief is temporary, and the infant becomes much worse over the next 24 to 48 hours. The foreign body reaction to the tube only adds to the edema and secretion already present. The flow of air or oxygen directly into the trachea serves to make secretions more dry, more sticky and tenacious. So it is apparent that the postoperative care is very important.

All authorities advise doing the tracheotomy over a bronchoscope or some laryngeal airway. Weinstein[5] discusses the removal of crusts and secretions from the bronchial tree by the use of a rubber catheter or bronchoscope introduced through the tracheotomy tube. Logan[6] warns against inserting a rubber catheter beyond the extent of the tube, and suggests the use of a nebulizer interposed between the source of oxygen and the tube mouth. He states this procedure for moistening the oxygen has seemed life-saving in many instances. In this group of cases, maintaining moisture has been a great problem. Moist saline compresses over the tracheotomy tube, steam directed into the oxygen tent, even instillation of a few drops of saline into the tube periodically, have been tried. The nursing care of a tracheotomized patient is increased a hundredfold and must be of the highest, most vigilant type.

Morgan and Wishart[3] state that tracheotomy should be done if there is no improvement in the patient, or he is growing worse one hour after admission. In this study, two major situations requiring tracheotomy were seen. One occurred when the initial examination revealed a child so ill he seemed unlikely to live long enough for the antibiotics to control the infection unless an airway were provided. The other developed when the patient continued to grow worse after adequate antibiotic blood levels had been present for 12 to 24 hours and had failed to control the infection.

Whatever the indications used, it is urged that the operation be not undertaken lightly, and that, when done, it be done by trained operators if possible. The most logical procedure by far is to make a diagnosis of acute infectious laryngotracheobronchitis early enough, and to start treatment early enough so that the need for tracheotomy never arises.

SUMMARY

A series of 332 cases of acute infectious laryngotracheobronchitis has been presented with some observations as to the incidence as it concerns sex, age and season. A discussion of the management is given with a plea for early diagnosis and institution of therapy.

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SILENT HEMOLYTIC DISEASE OF THE NEWBORN. (Gynaecologia, Basel, 127: 285, May 1949). The object of this study by de Vries was to investigate whether or not a Rhesus antagonism between mother and child might affect the blood picture of the newborn in other than proved cases of erythroblastosis fetalis. Obvious cases of this disease were excluded from this study. The author made hematologic studies in 70 apparently healthy full term Rh-positive newborn infants, showing a Rhesus antagonism with the mother. The hematologic results in first-born children and in the later offspring have been reported and compared with those of a control group of 115 normal full term newborn infants who did not show this antagonism. Based on the blood examination of newborn and the serologic examination of the mothers, the author concludes that characteristic hematologic changes may appear. These changes are considered the result of an immunization of the mother with the Rhesus antigen by the placental route. In the child a picture compatible with acute hemolytic anemia may be produced. A correlation between the serologic changes in the mother and the abnormal blood picture in the child could not be demonstrated. The frequency of these cases of silent hemolytic disease of the newborn due to a Rhesus antagonism has been calculated to be approximately 2 per cent of all births. A clinically fully developed case of erythroblastosis fetalis occurs about once in 400 deliveries.—*Journal A.M.A.*

CONGENITAL ANOMALIES OF THE ESOPHAGUS*

Report of Four Cases

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Malformations of the esophagus are relatively uncommon.[1] Hirschsprung saw 14 cases in 16 years, Brennemann saw 3 cases in one year, and Schukowsky saw 1 case in 50,000 newborns. Parmelee, a writer, saw 2 cases in 15,000 babies in Cook Co. Hospital, Chicago, in 7 years. Cautley saw 1 case in 25 years.

Cautley[1] subdivides the malformations of the esophagus into 8 groups:

1. Complete absence of the esophagus.
2. Double esophagus with reunion at the lower end.
3. Diverticula or pouches.
4. Cysts.
5. Tracheo-esophageal fistula without atresia.
6. Congenital dilatation, mostly secondary to spasm or stricture.
7. Atresia without fistulous communication with the trachea.
8. Atresia with the lower end of the esophagus opening into the trachea and rarely into the bronchus.

All except the last group are rare. The first group is seen in monsters. The second, third and fourth groups are extremely rare and are seldom diagnosed during life. The sixth group is rare but 6 cases are on record to the year 1917. The sixth one or congenital dilatation was seen in 57 cases. This type consists of partial occlusion of the lumen by a fold of normal mucous membrane or a simple reduction of the size of the esophagus at one point, especially found at the upper or lower end. The eighth group is the most common as 75 per cent of all cases are of this type.

Until 1946,[2] 400 cases of congenital atresia with tracheo-esophageal fistula were on record. The esophagus and trachea develope from the primitive foregut but the differentiation from each other is not a simple process of budding.[3] There is a complex combination of differing rates of growth which normally results in separation of the structures not only by downward growth of the tracheal bud but also an upward growth of the walls of the primi-

*Read before the staff meeting of the Wilkes-Barre General Hospital, Wilkes-Barre, Pa., February 2, 1950.

tive gut. These unite to form an intervening septum. If the latter is incomplete or faulty an anomaly results.

The symptoms encountered in the commonest types are similar. Babies[1-5] at birth are normal except for excessive amounts of mucus in the mouth. This continues and with the taking of liquids the baby regurgitates mucus and liquids after some feedings and finally after all. Coughing, cyanosis and respiratory distress is shortly encountered. Meconium stools are passed until the bowel is emptied which takes several days. The abdomen clinically shows a fullness in the epigastrium due to air in the stomach. This is seen in the cases where the fistula is present. A gavage tube will not pass into the stomach. X-ray examination shows a complete obstruction to the passage of the tube usually at the level of the fourth thoracic vertebra. The stomach is seen distended with air. If the child lives long enough it will show emaciation from dehydration and inanition and finally death in the second week. This is from a bronchopneumonia caused by aspiration of the stomach contents into the lungs or spilling of mucus into the trachea from the esophagus.

Treatment has been unsuccessful for the most part. The operation of choice is that of anastomosis[4] between the upper and lower segments of the esophagus. There must be no more than two cm. separation of the ends in order to perform it. Two stages are usually necessary. In 3 years[6], 7 infants with fistula were operated upon at Vanderbilt University. One was successful and living until 1944.

CASE REPORTS

Case 1. J. G., male, aged one week, a private patient, was admitted to the Wilkes-Barre General Hospital October 25, 1948, with the symptoms of vomiting and much mucus in the throat. The child was of normal birth, over 7 pounds, but with much mucus in the throat. On the third day he began regurgitating liquids. The following day he looked badly and, believing there was pressure from an enlarged thymus, he was x-rayed at the hospital. Both the chest and neck were negative. For a couple of days the child seemed improved in spite of regurgitating of some fluids. On the seventh day all fluids and much mucus were expelled. Admission was advised at once.

Physical examination revealed nothing except emaciation. A gavage tube was passed to introduce fluids into the stomach but an obstruction was encountered. On October 25 an x-ray-barium feeding revealed a stenosis at the middle and upper one-third of the esophagus. The stomach tube was obstructed at this point and above this the esophagus was dilated. The heart lay to the right side of the chest giving the appearance of a dextrocardia. There was gas in the stomach.

A laryngoscopic examination on October 29 revealed a normal larynx. From the upper end of the esophagus a large amount of mucus was removed. A short rubber catheter was inserted into it and at a distance of 1 cm. an obstruction was encountered. The baby was kept alive on hypodermoclysis of saline as all liquids were promptly regurgitated, mucus was expelled or aspirated many times daily. At first this was thick and later watery, blood-tinged or brownish in color. All bowel movements were of meconium. Plans were being made to take the child to Philadelphia for surgery. The temperature arose to 105° F. The patient became worse, developing râles at both bases of the lungs. He died November 2, 1948, fourteen days old.

An autopsy performed revealed an emaciated baby. The heart was slightly to the right and the trachea contained a small amount of mucus. Just above the bifurcation of the trachea was an opening into the lower part of the esophagus. The lungs showed very little air in the lower lobes. The upper part was enlarged to 2½ cms. in circumference and was occluded just above the point at which the lower part of it opened into the trachea. All leaflets of the heart were soft and normal. The ductus arteriosus and foramen ovale were open. The heart showed an anterior prominence of the right side and a posterior position of the left heart. The stomach was dilated and contained a small amount of mucus. The mucous membrane of the small intestines was flat and contained air and bile-stained semisolid material. The large bowel contained air only. The chief pathological findings were congenital atresia of the upper part of the esophagus and fistula from the trachea into the lower part of the esophagus, central prominence of the right heart, bronchopneumonia in the lower lobes, absence of fecal matter in the colon.

Case 2. K., baby girl, was admitted by normal birth October 2, 1943, and died October 19, 1943, seventeen days old. It weighed

7 pounds. From birth it was unable to retain any swallowed food and became very cyanotic.

An autopsy revealed the esophagus to be completely closed off just above the level of the bifurcation of the trachea. The remainder of the gastro-intestinal tract and other organs were normal. This was a case of simple atresia.

Case 3. A. E., male, aged 6 years, was admitted for the first time April 10, 1936, and discharged the next day with complaints of difficulty in swallowing. Up to one and a half years of age he vomited most of his feedings. Since then foods were ingested without dysphagia but he sometimes vomited small amounts. Physical examination was negative.

The esophagoscope was passed without difficulty to the junction of the middle and lower one-third where the lumen was narrow but finally passed into the stomach. This stricture was dilated on 5 different admissions. This was a case of congenital stenosis.

Case 4. M. D., female, aged 45, was admitted April 29, 1932, and discharged May 8, 1932, because of inability to swallow. In 1918 after the influenza she began having difficulty with swallowing and could eat only strained foods. In examination with the esophagoscope an obstruction by a web of tissue was found at the level of the cricopharyngeal muscle. This was dilated and on several other occasions in 1932. This was also congenital.

SUMMARY

1. A classification of the congenital defects of the esophagus has been given.

2. Pertinent facts about the rarity of the conditions have been given.

3. One example of four conditions has been explained with autopsy findings when death occurred. Only 4 cases are on record in this hospital since 1930.

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DISTURBED CHILD—DISTURBED FAMILY

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"Doctor, Johnnie is so irritable that he makes me nervous," says an anxious mother. "He is wetting the bed again. The teacher says that he doesn't seem to concentrate and he doesn't get along well with the other children. He used to mind me right away and be careful of his toys. His father is getting very upset too and blames me for not being able to handle him. I have read that there are no bad children, only bad parents. Should I take him to a psychiatrist or can you help me?"

This sort of problem is very familiar to the author, who met it first in pediatric practice and later as a psychiatrist in a child guidance clinic. In the former capacity, a lot of time was wasted with certain mothers. We were not clear as to just what is a disturbed child and what is a disturbed family. After watching children play and draw and listening to them talk, as well as listening to mothers and fathers, the following differential points became clearer:

1. The disturbed child has a short frustration tolerance. He is a poor loser. When the door sticks, for example, he keeps kicking it long after it opens. He finds it difficult to adapt himself.

2. It is difficult for him to form a positive relationship, especially with children his own age. He is apt to do poorly at school and use the formula, "If I don't try they can't say that I failed."

3. He is not well aware of his real feelings. He may be mad, but doesn't focus on the person responsible for his frustration, and displaces his hostility onto other people or things. He may be overconforming, eager to please. Such a child may be called "psychoneurotic." He presents a different problem from one who is simply temporarily frustrated by his environment and is expressing this in "reactive behavior." The latter knows who he is mad at. He will be greatly helped if the parents can let him express his feelings, and he can benefit from changes in his environment. When the parents change their attitude, he will change his more or less automatically. This is not true of the anxious, disturbed child.

4. The disturbed child may be very impulsive and directly hostile. If he happens to break the law, he will be called a juvenile

delinquent. A "psychopathic" reaction appears on the surface to be just the opposite from that of the anxious, disturbed child, since this child shows no evidence of feeling guilty. However, such defiance will be found to reflect even deeper distrust of others.

5. The disturbed child may exhibit many or few so-called neuropathic traits.* Instead of those mentioned, above, Johnnie's mother might have been concerned about nail biting, head banging, stuttering, finicky eating habits, restless sleep, phobias, etc. Or he might experience any one of a number of psychosomatic illnesses.**

6. He may have difficulty telling the difference between phantasy and reality. He may withdraw into an inner life of day dreams. If this reaction is marked it will resemble adult schizophrenia.

7. The disturbed child is always accompanied by a disturbed mother, who exhibits similar characteristics. It will usually be obvious to the doctor that it is difficult for her to be firm without being harsh and it is usually obvious that she is unable to let the child express his real feelings. She may or may not be conscious that she can not give the child much affection. In either case, this may be the basis for her feelings of inadequacy. Usually there is evidence that she is not getting much affection herself even if the home is not broken.

Not every reader will agree that the disturbed child is *always* accompanied by a disturbed mother. The latter may be disguised

*We interviewed several hundred mothers with children from ages 1 to 12 regarding behavior problems and found that in this unselected group the number of problems varied from one to six per child. Tempers, fears, jealousy and over-sensitiveness were found to increase up to age 4½, then began to subside. Anorexia was most common at 2½ to 4. Soiling and enuresis were found to decrease with age. Thumb sucking decreased as nail biting increased. Negativism reached its peak at 2½. Nail biting, anorexia, and overdependence occurred more frequently in children with poor physical status. The undersized or oversized child tended to show shyness or aggression. Excessive reserve or introversion were noted in children with low energy levels. Since some of these behavior problms occurred in all of the children we feel that it is hardly sensible to regard them as essentially neuropathic. They are found in both disturbed and relatively normal children. (ARCH. PEDIAT., 63:216, May 1946).

**In an article "Allergy in Childhood" (ARCH. PEDIAT., 64:192, April 1947) we stated that in 30 of the 50 asthmatic children studied, emotional factors were important in initiating or increasing the severity of the attacks. On the other hand, about half of the parents reported definite emotional improvement after the allergic factors were controlled. Therefore, we emphasized that both the emotional and immunological factors are important and that neither should be neglected.

as the oversolicitous mother, for example. That she is strangling the child with her apron strings, that she holds up impossible standards, or that the parents' too rigid discipline stems from their own anxiety about the child's social adjustment may not be obvious at all. The mother may have a deep "inferiority complex" and this may be reflected in feelings of inferiority in the child. She may have a tremendous need for affection and smother him. The more aggressive mother will need to dominate others, but this may be done indirectly and it will not be obvious either. How can the parents help the child develop inner standards if they are secretly defiant of social institutions?

To summarize, the disturbed child does not seem to feel good about himself. His treatment of other children and adults reflects this. This leads directly to the disturbed family. The child's self-respect depends on others. At first, as a small child, he can only value himself if others value him. He has no other means of determining his worth. He learns from experience. If mother smiles he will tend to repeat the behavior that brought forth the smile. If she frowns or spanks in disapproval, he will tend to avoid this behavior. If he can not be sure whether she will smile or frown, if she smiles one time and frowns the next in reacting to the same behavior, if he can not be sure where she draws the line, or if the line is wobbly, then his character will reflect this, because the line that the parents set down turns out to equal the child's conscience. Speculation as to how this may come about is very interesting but beyond the scope of this paper. Also, whether mother smiles or frowns depends upon her own experience. There are important social implications here which go back to the parents' own relationship to authority, affection, sex and self-expression in their own childhood. We have found that it is difficult for parents to be firm if they did not experience firmness without harshness in their own childhood. Neither is it easy for them to allow the expression of feelings if they had no experience of this in childhood. If they try to "overcompensate" for this they will defeat their purpose. It is well-known that when one parent is strict and the other lenient the child may become disturbed. We feel that lack of consistency or conflicting feelings in the individual parent is even more important. The child can adjust even to a harsh parent if that parent is consistent.

Pediatricians as a group have always been especially interested in prevention of illness. This turns out to be an extremely complex problem when applied to emotional illnesses.

The crux of our problem then is what to do. Not all disturbed children can be referred to child psychiatrists, psychoanalysts, psychologists or child guidance clinics. A pediatrician or general practitioner may not feel morally justified in taking such a case himself any more than he would operate on a ruptured appendix without considerable experience. Even if facilities are available for specialized help for the disturbed family, he may sense that the parents are not ready for it. We mentioned that we had wasted a lot of time in pediatric practice discussing behavior problems with certain mothers. For one thing, we did not at first differentiate one mother from another. Our experience was that if the family is very disturbed there is little that the non-specialist has to offer. This is most obvious if the mother is psychotic. The disturbed mother simply is not in a position to use any help no matter how well intended. Of course, she wants advice, and yet it is our invariable experience that no advice will help. We feel that it is just as sensible to tell such a mother to go home and lower her blood pressure as it is to reassure her, tell her not to worry so much or to give the child more affection (as if she could pour this out just because it would be good for him!).

This is the doctor's dilemma: The family is disturbed. The mother asks for help. Traditionally that is what the doctor is there for. He would also like to be of help. The mother will often blame the child or the school. We feel that it is unnecessary and not helpful for the doctor to blame her. She already blames herself, even if she does not say so, and it is difficult to react in such a way that she will leave the office with a little less anxiety than she came in with. If a consultation or a referral is recommended, we feel that the consultant or psychiatric intake social worker will be in a better position to help the mother find out what she really wants to do and what the person or agency has to offer.

Environmental manipulation has been tried and found wanting in many of these cases. Institutionalization or foster home placement may seem indicated, especially if the child has a developmental defect in addition to problem behavior. However, this leaves the intra-psychic part of the conflict untouched.

When we were able to be direct with the mother as to our limitations (which we were reluctant to admit) and the complexity of the problem and to help her verbalize her feelings about coming for help and about conduct, rules, reputation, and her own experience with authority, and when we could encourage her to talk about the child, herself, and her husband without adding to her feelings of inadequacy, a start had been made that she might follow up then or at a later time.***

We see the "psychopathology" in the relationship between the child and the dominant adults in his environment. The disturbed child is in a vicious circle. His reactions annoy the parents and their retaliation causes more resentment in the child, with a corresponding reaction which the parents dislike even more. They will call the child stubborn or persistent depending on their own likes and dislikes.

Ideally such a child should have the experience of relating to a mature adult, who will be able to be firm without being harsh and who will accept the child's feelings (including uncertainties about sex) and help him bring them out. This may be possible only with direct psychotherapy. Ideally, the parents with help will gradually become the mature adults who can give the child the feeling that they are on his side. They will be able to react positively. They will let the child gradually assume self-direction in order to prepare for his adult role. They will have the great satisfaction of fulfilling their own roles. The difference in their attitudes might be illustrated by the familiar story of the two men working on a building. One said that he was carrying a hod, the other said, "I am building a cathedral!"

***Some 20 examples of such a non-lecturing approach are contained in an article "Improving Parent-Doctor Relationships" in ARCHIVES OF PEDIATRICS, 64:630, December 1947. This is not suggested as a technique to follow, but is one way a "you and me" relationship can be started.

AMINOPTERIN IN LEUKEMIA

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Since the synthesis of aminopterin (4-aminopteroyl-glutamic acid) in 1947[1] which was found to be a strong antagonist of folic acid, its effect in the control of leukemia has been on trial with promising results.

Faber[2] reported that out of 60 children with acute leukemia who received aminopterin, or one of the other analogues of folic acid, 50 per cent showed hematologic improvement. Dameshek[3] concluded that one-third of his 35 patients with acute or subacute leukemia, who were given antagonists of folic acid, showed remissions. Faber et al.[4] administered aminopterin by intramuscular injections to 16 children with acute leukemia. Ten showed marked improvement, 2 unimproved and 4 died. They used to give a dose of 1 mgm. daily for the first few days followed by smaller doses at less frequent intervals according to the progress of the condition. In the case here reported, two doses each of 0.5 mgm. with a clear day in between proved to be rapidly fatal.

CASE REPORT

Boy, 3½ years old. His birth and development have been within average normal. Except for few attacks of enterocolitis his past history was noncontributory. About 9 days before coming for medical examination he had septic rash over his body for which he received local treatment with marked improvement. Six days later the rash recurred and this time the patient became feverish and had swellings of his neck.

Physical examination on August 7, 1949 showed a fairly developed and nourished boy weighing 14 Kgs. He was moderately ill and pale with a temperature 39.3°C. There was septic rash irregularly distributed all over the body. The tongue was coated and there were ulcerations on both tonsils. The cervical lymph nodes were moderately enlarged while the axillary and femoral groups were slightly swollen. Moderate hepatomegaly and splenomegaly were found. Heart showed systolic pulmonary murmur and lungs were clinically free. For personal reasons the parents refused hospitalization.

Penicillin 50,000 units every 3 hours was started. Blood picture done on the next day showed hemogloben 52 per cent (Sahli), R.B.C. 2,790,000, color index 0.96, W.B.C. 230,000 per cmm. Differential count: Polys 3 per cent (2 per cent stabs and 1 per cent segmented) and lymphs 97 per cent. On August 9, 1949, the child looked more pale with some peticheal hemorrhages on his limbs and ecchymosis of the soft palate. The torniquet test revealed decided increase in capillary fragility.

Aminopterin 0.5 mgm. was given intramuscularly. This was supplemented by vitamin B_6 50 mgm. intravenously, rubramin (vitamin B_{12}), vitamin C 500 mgm., liver extract and vitamin B complex.

On August 11, 1949 the throat condition was better but ecchymosis was found at the sites of injections. The child lost weight, became more pale and restless with insomnia and difficult respiration. The second dose of aminopterin was given and next day the condition was worse with intense pallor, marked difficulty in respiration, severe colicky pains and melena. Hemoglobin fell to 15 per cent and the white cell count to 15,200 per cmm. Blood transfusions were given but the patient died on the morning of August 13, 1949.

COMMENT

In spite of using small doses of aminopterin at infrequent intervals in treating such a severe case of acute leukemia, yet the hematologic remission occurred extremely dramatically and rapidly having followed the second dose and was accompanied by severe toxic reactions that ended fatally.

It is suggested that until the synthesis of compounds which will elicit minimal damage to the body but retain the beneficial therapeutic effects, every individual case should be carefully tested for the degree of response and toxic reactions when aminopterin is started.

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PEDIATRICS HALF A CENTURY AGO

From time to time the Archives, which was the first Children's Journal in the English language, will reprint contributions by the pioneers of the specialty over fifty years ago. It is believed that our readers will be interested in reviewing such early pediatric thought.

GASTROINTESTINAL TOXEMIA*

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Cincinnati.

Gastrointestinal toxemia as differentiated from autointoxication is a systemic intoxication, produced by poisons formed in and absorbed from the gastrointestinal canal. Autotoxins, excreted into and afterward absorbed from the intestinal canal, cannot, therefore, be classed as intestinal toxins.

Our knowledge of the toxins, which contribute to intestinal intoxication, is not as yet upon a very satisfactory chemical basis. We know, however, that the intestinal contents, even under normal conditions, are toxic, and we know, also, that under certain pathological conditions the toxins produced by the bacterial fermentation of foods in the intestinal canal very greatly increase this toxicity, with the result that a profound systemic intoxication is produced. Our present knowledge, however, is not as yet sufficient to make it profitable for us to attempt to differentiate clinically, between the symptom groups produced by normal and abnormal intestinal toxins.

INTESTINAL TOXINS

The poisonous albumoses, which are the intermediate bodies formed in the digestion of albuminous food stuffs, may be mentioned as contributing to the toxicity of the intestinal contents, but these bodies, under normal conditions, are robbed of their toxicity, in their passage through intestinal epithelium and liver cells, during the process of absorption. The body is, therefore, carefully guarded against intoxication from this source. It may be, however, that when these protective mechanisms fail, through

*Read before the Sixteenth Annual Meeting of the American Pediatric Society held at Detroit, Michigan, May 31, 1904.
Reprinted from ARCHIVES OF PEDIATRICS, 21: 666-675, September 1904.

disease or functional disturbances of these filtering organs, these bodies may act as toxins.

Bacterial fermentation is the great source of intestinal toxins. It is possible that the poisons produced by bacteria in the intestinal canal may have their origin from three different sources.

(1) The components of dead bacteria may furnish a certain amount of proteins, some of these bodies we know to be poisonous, as for example, tuberculin, which is a protein of the tubercule bacillus. The bacillus of glanders, and other bacilli also contain poisonous proteins, and it is not impossible that poisons of this type may at times be a factor in producing intestinal toxemia. The rôle, however, which these bodies play in intestinal toxemia has not as yet been determined, and is probably not very great.

(2) Living bacteria in the intestinal canal, may and do excrete ferments or toxins, capable of producing the most profound nervous symptoms. These specific toxins of bacteria are believed to be very potent factors in producing intestinal toxemia. It is evident that the character and virulence of these toxins will depend largely upon the microorganisms producing the fermentation, since certain microorganisms are capable of eliminating much more virulent toxins than others. Whether all of these cell toxins belong to the ferment class is a question as yet undecided. Pathologists, at the present time, incline to the view that the specific toxins are closely allied to, if not identical with, the ferments.

(3) Substances produced by bacteria from the culture media are possibly the most important source of intestinal intoxication. Among the poisons of this class, the ptomains probably hold the most important place. These basic compounds, resembling the alkaloids in chemical structure, are capable of producing the most severe systemic intoxication. The virulence of the ptomain formed depends not only upon the microorganism, but also upon the character of the food material in which it is growing. Certain food materials, such as cheese, milk, meat, and other albuminous foods, when acted upon by certain bacteria, may become very poisonous owing to the development of poisonous ptomains.

While ptomains are the most poisonous, and so far as the etiology of intestinal toxemia is concerned, the most potent of the transition products produced during the process of putrefaction,

yet there are a large number of other bodies produced in this way, which may also be factors in producing intestinal toxemia. Among these bodies may be mentioned, indol, skatol, phenol, cresol, leucin, tyrosin, ammonia, sulphuretted hydrogen, volatile fatty acids, oxalic acid, uric, and the xanthin bodies. Of these bodies, however, it must be said, that indol is probably the only one, whose etiological relationship to nervous symptoms has been satisfactorily demonstrated. Herter and others have recently shown that indol, one of the most constant and readily absorbed products of the bacterial fermentation of albuminous food stuffs in the intestinal canal is toxic, and capable of producing headache, and increased nervous excitability. It is not improbable, therefore, that this body may at times, under the conditions named, contribute to the production of these symptoms.

Indirect Etiological Factors. Constipation is the most important predisposing factor of both acute and chronic intestinal toxemia. It acts by retarding the passage of food materials along the intestinal canal; this gives time for hyperfermentation, and for the production of toxins by bacterial action on the intestinal contents.

Too much food, indigestible food, and food that has already undergone bacterial fermentation, may also be important factors in producing, or in prolonging, either an acute or chronic intestinal toxemia.

Lack of fresh air and exercise are also important predisposing factors.

The digestive idiosyncrasies of the individual are predisposing factors which manifest themselves not infrequently. These idiosyncrasies are sometimes made manifest by the taking of such foods as milk, eggs, oatmeal, shell-fish, strawberries, acids and wines. One of the most common of the nervous syndromes developed in this way is urticaria. This symptom group is not uncommonly associated with an acid fermentation in the intestinal canal and may in certain instances be classed as an acid intoxication of intestinal origin.

In studying the etiology of intestinal toxemia, it is necessary to bear in mind the important rôle which the liver plays in protecting the body against intestinal toxins. These bodies can reach the general circulation, and thereby produce systemic intoxication,

only by passing through the liver; and in leaving the intestinal canal these bodies pass through the portal vein, and thence through the liver to be worked over by the liver cells, and filtered through by way of the hepatic vein, and lymphatics to the general circulation. In passing through the liver, however, these intestinal poisons are under normal conditions rendered harmless. This socalled filtering function of the liver stands guard between the poisons absorbed from the intestinal canal, and the general circulation.

One may suppose that as long as the toxins in the intestinal canal are not greatly increased in quantity, and as long as the filtering function of the liver is intact, the intestinal toxins cannot produce systemic intoxication, and one may also suppose that systemic intoxication may be produced by failure on the part of the liver to perform its function of filtering the poisonous blood in the portal vein, or from a great excess of intestinal toxins, which may so overwhelm the liver that these poisons find other channels of entrance into the general circulation.

It is well to keep these facts in mind, since in some instances the liver itself may be primarily at fault in chronic intestinal toxemia. This organ, therefore, must be kept under supervision in the treatment of all chronic neuroses, which are supposed to be either wholly or partly caused by intoxications from the intestinal canal.

Chronic intestinal toxemia may also be an indirect cause of nervous symptoms, by the profound changes it sometimes produces in the blood, contributing as it does to the production of chlorosis, and other forms of chronic anemia. These anemic conditions may in turn cause malnutrition of nerve centres, and in that way produce chronic nervous irritability, and the long chain of nervous symptoms which are not uncommonly associated with profound anemias.

Chronic appendicitis, especially in the adult, is not an uncommon cause of intestinal toxemia. This condition may exist for a long time without being marked by distinct attacks of acute appendicitis. In these cases the symptoms of intestinal toxemia, such as headache and general nervous irritability, may be associated with a mucous colitis, tenderness in the region of the appendix, an occasional colic, and ofttimes a sensation of weight and discomfort in that region on active exercise.

ACUTE INTESTINAL TOXEMIA

Acute intestinal toxemia is more common in the infant and young child than it is in the adult. This greater susceptibility to the acute forms of intestinal toxemia is probably due to a number of causes, the most important of which is the great irritability and the immaturity of the nervous system of the child. This instability of the nervous system of the child makes it possible for slight disturbing factors to produce maximum results. A small quantity of poison absorbed from the intestinal canal may, through its action on the susceptible nervous system, produce high fever, convulsions, and other pronounced nervous symptoms, while the same quantity of poison might be easily resisted by the stable nervous system of the adult.

It is also true that severe albuminous fermentations capable of producing virulent toxins are more common in the child than they are in the adult. This may be due to the fact that the hydrochloric acid function of the stomach is not as well developed in the young child as in the adult, and therefore not capable of exercising the same control in preventing intestinal fermentations. It may also be possible that the filtering function of the liver, which is at all ages one of nature's safeguards against intestinal toxemia, is not as well carried out in the child as it is in the adult. But whatever may be the explanation, acute intestinal toxemia is much more common in the young child than in the adult.

While our knowledge of the poisons which produce acute intestinal toxemia is very unsatisfactory, yet there is no doubt but that such a toxemia exists, and that it is one of the most important factors in producing nervous symptoms in the young child, and a somewhat less important factor in producing nervous symptoms in the older child, and the adult. Acute intestinal toxemia occurs so commonly in the infant and young child that we are justified in suspecting this cause, where no other apparent cause presents, as a factor in producing sudden rises of temperature, and acute convulsive disorders.

The nervous symptoms which result from acute intestinal toxemia, may vary in severity from a slight fever, with exaggerated reflexes, to a high fever and convulsive disorder so severe as to produce death. Every physician recognizes the importance of acute intestinal toxemia as an etiological factor in the pro-

duction of dangerous nervous symptoms in the infant and child, and everyone has seen these convulsive disorders followed by high fever and unconsciousness, quickly relieved by cathartic medication, and cured by intestinal antiseptics and diet.

CHRONIC INTESTINAL TOXEMIA

Familiar as we are with acute intestinal intoxications, we are slow to recognize the importance of chronic intestinal intoxications, which are produced no doubt by the same intestinal toxins, absorbed in smaller quantities and over a longer period of time.

As the child gets older and the nervous system develops, and acquires greater powers of resistance against these toxins, then the acute intoxications become less, and the chronic intoxications more important, so that in the older child, these severe forms of acute intestinal toxemia are infrequent as compared with chronic intestinal intoxications.

It is the chronic form of intestinal intoxication to which I wish to call special attention, because its great importance as an etiological factor in producing nervous symptoms in children is commonly overlooked.

Chronic intestinal toxemia may be associated with diarrhea, but is not uncommonly associated with constipation. It must be remembered that constipation may exist even when the child has a movement from the bowels every day, or even two or three movements. These movements may be fragmentary and therefore incomplete, or they may be hard and dry showing that they have remained in the intestinal canal twenty-four or more hours longer than they should.

In order to prevent hyperfermentation, and increased absorption of intestinal toxins, the food materials must not be retarded in their passage through the intestine, and when ejected should be moist and have the appearance and form of the normal intestinal evacuation.

So important, do I believe, is the rôle played by chronic intestinal toxemia in the production of neurotic diseases in the child, that I invariably begin the treatment of nervous diseases whatever the symptom group may be, by a careful investigation of the intestinal canal, and throughout the treatment of these cases I give careful attention to any abnormalities of digestion.

The child should be fed upon food carefully adjusted to its digestive capacity, and there should be no retardation of food stuffs in their passage through the intestinal canal.

Chronic intestinal toxemia is probably a factor in the production of a large group of nervous symptoms, and may, as I believe, aggravate the symptoms of certain neuroses, which are produced by etiological factors entirely foreign to the intestinal canal. Among the symptoms which may be produced or exaggerated by intestinal toxemia may be mentioned, malnutrition, anemia, headache, general malaise, fever, heightened reflexes, convulsive disorders, restlessness at night, night terror, general nervous irritability, hysterical and neurasthenic symptoms, incontinence of urine, brachicardia, hyperesthesia, paresthesia, nervous anxiety, psychoses, and, in rare cases, a syndrome resembling meningitis.

The following case while somewhat unusual in the character of the nervous symptoms which it presents, may be taken as a good example of neurotic disease produced by intestinal toxemia.

SEVERE NERVOUS SYMPTOMS PRODUCED BY INTESTINAL TOXEMIA

Boy, age five years, has never been strong, has had stomach and intestinal trouble very frequently during his life. At the present time, he is thin, anemic, and has the appearance of being malnourished. During the past year he has been very nervous, and this nervousness has recently very greatly increased, so that at the present time he is irritable, cries on slight provocation, is very restless at night, and has certain peculiar nervous attacks, which led his mother to seek medical advice. These attacks come on suddenly with dizziness; the boy falls to the ground, and his mother thinks he does not lose consciousness, and is sure he has no convulsive movements. Some minutes elapse before the boy is able to regain his feet. These attacks are followed immediately by severe headache, and more or less nausea. Following these attacks, the boy is put to bed, and soon falls into a profound sleep, which may last some hours. From this sleep he awakes almost or quite as well as before the attack.

He has had in all, seven attacks during the last year, and three of them have occurred within the last two months. These attacks which seem to occupy the border land between migraine

and epilepsy have not only increased in frequency, but also in severity.

The family history throws no light on the etiology of these attacks. The father is phlegmatic, the mother is somewhat nervous, but there is no history of neurotic disease in the family.

A careful examination failed to show any reflex factors which might be etiologically related to this neurosis.

The mother says that for a long time the boy has not been normal in his intestinal canal. Diarrhea has alternated with constipation. There has been much flatulency. The boy has a fitful appetite, and craves food he should not eat. He has been fed almost anything, because "he ate so little," the mother thought "it would not hurt him."

This history strongly suggested the probability that the nervous symptoms might be due to intestinal toxemia.

An examination of the urine, which was high colored, and had a specific gravity of 1023, showed no albumin, no sugar, but a marked excess of indican.

Treatment. A dose of castor-oil, followed by a diet, carefully regulated to suit the patient's digestive capacity; active life in the open air; a diastase and iron preparation after meals. Under this treatment the boy's general health gradually improved. He gained slowly in strength and weight. His general nervous irritability, which was greatly improved from the beginning of the treatment gradually disappeared. He never had any of his peculiar attacks after the treatment was begun. Three months later he was discharged well.

Intestinal toxemia, acute and chronic, is not an uncommon complication of other diseases, such as typhoid fever, malaria, tuberculosis, and chronic diseases of the gastrointestinal canal.

As a complication this condition is probably met with more commonly in the convalescence from typhoid fever than in any other disease. The physicians unjustifiable fear of cathartics in this disease is ofttimes prolonged into the period of convalescence, and as a result, fecal accumulations occur, which result in an intestinal toxemia which prolongs the period of convalescence many weeks.

The urine furnishes valuable evidence of the existence of intestinal toxemia, and ofttimes our attention is called to this con-

dition by the presence of an excess of indican, and the ethereal sulphates in the urine. The presence of these substances in the urine is sufficient reason to suspect a hyperfermentation of albuminous food stuffs in the intestinal canal, and also usually means the retardation of these food stuffs in their passage through the canal, but the absence of indican does not rule out intestinal toxemia, since we may have severe forms of intestinal toxemia in which indol is not an etiological factor.

The etiological importance of the vegetable organisms in producing intestinal toxemia, must not cause us to altogether overlook the possible rôle which animal parasites may play in these pathological processes. In the present state of our knowledge, however, it is not possible for us to make any positive statements as to the exact rôle, which intestinal worms play in producing gastrointestinal toxemia. Lynch in Grancher and Comby's "Maladies de l'Enfance" says that intestinal worms may be responsible for a large group of toxic symptoms, such as urticaria, ringing in the ears, syncope, vertigo, palpitation of the heart, insomnia, mental anxiety, hypochondria, general nervous irritability, fever, delirium, and convulsions.

While this group of severe toxic symptoms may be associated with intestinal worms, it does not necessarily follow that they are produced by the absorption of poisons which have been excreted by them. Lynch himself points out the possibility of these symptoms being produced in part at least, by the secondary fermentations, which the presence of these parasites excite in the intestinal canal, and notes, also, the possibility of severe symptoms being produced, reflexly and mechanically by their action.

Leukart observed that the ascaris lumbricoides excreted a poison capable of producing toxic symptoms. Huber, von Linstow, Chanson, and Raillet, state that this same worm contains an irritating substance capable of producing a toxic effect on the human organism, and a number of other French authors state that this worm excretes an irritating and convulsive substance. Cao, on the other hand, after carefully investigating the subject, concludes that the evidence at the present time does not justify us in attributing toxic symptoms to the action of poisons excreted by intestinal worms.

While there is considerable difference of opinion as to the

etiological relationship which exists between animal parasites and intestinal toxins, it seems to be rather generally conceded that these parasites may either directly or indirectly produce intestinal intoxication. In this connection the following case is of interest:

SEVERE GENERAL CONVULSIONS PRODUCED BY NEMATODES IN THE INTESTINAL CANAL

I was called in consultation to see a girl, twelve years of age, who had been having convulsions for several hours. She was a strong, healthy German, with no tendency to neurotic disease. After a few days of slight indisposition, on the part of the intestinal canal, she suddenly had a severe convulsion. On my arrival I found that the physician in attendance had been working with her for some hours, and that during this time, she had had a number of severe convulsive seizures. In the intervals between the convulsions she was unconscious and had considerable muscular rigidity.

After controlling the convulsions with chloroform, the urine, drawn with a catheter, was found to be normal. Sulphate of magnesia was given by the mouth, and by rectal injections. Some hours later a large ball of round worms (ascaris lumbricoides) was passed with a large amount of fecal matter, and very soon thereafter the patient was restored to consciousness, and the next day was well.

There can be no doubt but that this was a case of intestinal toxemia. The child's age, previous good health, and stable nervous system speak against the reflex origin of these convulsions; and I may further state that while it is impossible for one to exclude absolutely other causes of intestinal intoxication, the discharges from the intestinal canal were not of such a character as to indicate that the poisons were produced by the fermentation of the intestinal contents.

CLINICAL-PATHOLOGICAL CONFERENCE

WILLARD PARKER HOSPITAL, NEW YORK
Meeting held December 20, 1949
DR. PHILIP MOEN STIMSON, presiding.

ACUTE ANTERIOR POLIOMYELITIS

DR. MILLER presented Case No. 4543, a 7-year-old white boy, who was admitted on October 19, 1949 to this hospital with a history of pain in the back and thighs beginning on the previous day. On the day of admission these complaints were worse, and headache, pain and stiffness of the neck appeared. Child was febrile.

Physical Examination on Admission revealed a fairly nervous, well-developed, well-nourished, white boy showing occasional muscle twitching and jerky respiration. His neck and back were stiff and there was bilateral hamstring tightness. Spinal tap showed 700 white cells, 83 per cent polys.

On the morning of October 21, 1949, he developed shallow, rapid respirations with use of accessory respiratory muscles, and he was put into a respirator. Secretion in his pharynx appeared to be increased. He became drowsy and was maintained on intravenous feedings. Chest packs, nasal oxygen, suction and penicillin were used. Irregularities of heart rate were noted on the same day. An electrocardiogram on October 22, 1949, showed "sinus arrhythmia."

On October 22, 1949, he was comatose and vomited much "coffee-ground" material. His blood pressure tended to fall and neosynephrine injections were given frequently. He became markedly distended. His color became worse and did not improve in spite of therapy and at 5:50 P.M. on October 22, 1949, he expired.

Necropsy. DR. JUROW presented the gross findings. The body was that of a well-nourished, white boy of seven. The mucous membranes were moderately cyanotic and there was dry, black material about his nose and mouth. The lungs showed extensive areas in the right and left upper lobes and scattered areas in the lower lobes which were deep red in color, firm and had markedly

diminished crepitation. Sections from these areas sank in water. The remaining parts of the lungs were congested and edematous. Much black colored, mucoid fluid was present in the trachea, bronchi and larger bronchioles. The intestines were greatly distended with gas, and segments of the ileum contained pasty, black material. The stomach contained much black mucoid material and, when this was wiped away, showed streaks of fresh blood over the mucosa. No defects in the stomach wall could be detected. The brain showed only edema and congestion grossly. No other gross abnormalities were detected.

Discussion. Dr. Stimson. Was there edema in the cord?

Dr. Jurow. The child had much edema of the brain, but none could be seen in the cord.

Microscopic Findings were projected by Dr. Dolgopol. All parts of the spinal cord, from the cervical down to the sacral, showed extensive damage to the gray matter of anterior and posterior horns (loss of most nerve cells, glial nodules, diffuse gliosis). Perivascular cuffing was present in the gray and white matter. In the medulla extensive degeneration of neurosis and glial reaction were present involving nuclei of many cranial nerves and the reticular substance. The midbrain was severely damaged. A number of foci were also found in the motor cortex. As a result of severe central respiratory damage (reticular substance, some of the nuclei of the tenth nerve) and damage of respiratory musculature, there was extensive bilateral atelectasis. There was no significant degeneration of myocardium. The gastric mucosa was not damaged, and the "coffee-ground" vomiting was due to trickling of blood from the nasal catheter into the stomach.

Discussion. Dr. Schwartz. Any x-rays in this case?

Dr. Seanor. No x-rays in this case.

Dr. Stimson. How soon after admission was oxygen started? Sometimes patients receive oxygen before they need it. Something can be done about edema. Ten per cent glucose does no harm. It may counteract edema.

TUBERCULOUS MENINGITIS

Dr. Humphreys presented Case No. 4846, a 50-year-old white man, who was admitted to this hospital on November 28, 1949, with a history of rigidity of the neck, loss of deep tendon reflexes

and abdominal reflexes and a temperature of 102° F. noted on November 27, 1949. Spinal tap revealed fluid at 44 mm. of water pressure, slightly cloudy and containing a pellicle which showed many acid-fast bacilli on smear. The fluid contained 310 cells, sugar 46 mg.%, protein 88 mg.% and chlorides 575 mg.%. Additional history from his wife disclosed that he had had an attack of "influenza" in September 1949, and had had frequent, severe headaches from the time of recovery from that illness to the time of admission. There was no history of tuberculosis in the patient or family.

Physical Examination on Admission revealed a well-developed, moderately dehydrated man who appeared acutely ill and was irrational. He had nuchal rigidity, a positive Kernig, absent cremasteric and abdominal reflexes, absent deep tendon reflexes in the upper extremities and ankles. Spinal fluid showed pleocytosis, low sugar and acid-fast bacilli.

Streptomycin, intramuscularly and intrathecally, promizole, and infusion were begun on November 29, 1949. The patient sank into deep coma and his color became bad. He vomited and, on suctioning, fresh blood was obtained. Oxygen was given, and at 2:00 A. M. on November 30, 1949, the patient expired.

Necropsy. Dr. Dolgopol presented the gross specimens. A number of pin-point tubercles were present over the hemispheres. Only one layer tubercle was found in the right motor area. At the base of the brain, in the area of the chiasm, there was much gelatinous looking exudate. No tuberculomas were found on sectioning of the brain. In the lungs, the entire tissue on both sides was riddled with pin-point-sized tubercles. A caseous focus, about 1 cm. in diameter, was present in the right apex, but no caseous or calcified lymph nodes were found in the hilar region. A number of larger tubercles were found in the kidneys. A large caseous focus was found in the right adrenal. Tubercles were present on the serosa of the right lobe of the liver, abdominal aspect of the right diaphragmatic wall, on the parietal serosa of the anterior abdominal wall, on the surface of the spleen. The prostate was large and one section was almost completely caseous. The lesion of the right apex appeared to be a primary focus which was not old and did not come to complete healing. The myocardium was flabby and friable.

Microscopic Slides were projected. Brain: The meninges showed scattered miliary tubercles and one larger caseous tubercle, older in age. Much cellular and fibrinous exudate and large areas of degenerated epithelioid cells were found at the base of the brain. The caseous lesion of the right adrenal was also older than the miliary tubercles of most organs. Prostate was riddled with large caseous areas. A polypoid mass of tubercles was protruding into the lumen of one of the veins in the capsule of the prostate. Such findings explain the development of hematogenesis spread of tuberculosis. Single tubercles were found in the pancreas (this is very rare) and in the myocardium, which is an infrequent finding. The myocardium was fragmented, even away from the tubercle. Death was probably due to toxic degeneration and extensive fragmentation of the myocardium, rather than to tuberculous meningitis.

VISUAL DISTURBANCES IN TUBERCULOUS MENINGITIS TREATED WITH STREPTOMYCIN. (Wiener klinische Wochenschrift, Vienna, 61: 407, July 1, 1949). Mejer reports serious visual disturbances in 8 of 52 children with tuberculous meningitis during or after treatment with streptomycin. A more or less advanced atrophy of the optic nerve was the cause of the visual disturbance in 5 instances. Optochiasmatic arachnoiditis was suggested by the clinical or pathologic signs in 4 of the children, 3 of whom had atrophy of the optic nerve. Temporary sudden blindness occurred in 1 girl aged 5 years and 1 boy aged 3½ years, but vision was restored to normal several days later. In these 2 cases the visual disturbance was considered as a symptom of acute internal hydrocephalus. These tuberculous changes of the brain may be considered as sequelae of the treatment with streptomycin only as far as the antibiotic delays the formerly more acute course of the disease by changing it into a more subacute or chronic form. Clinical observations in tuberculous meningitis may thus become possible. These were not possible before treatment with streptomycin was practiced. The visual disturbances in the last 2 cases may be the result of a cortical pressure effect.—*Journal A.M.A.*

"There's no such animal," he cried!

My friend and I were picking the ponies one day when I started telling him about a *sure thing* I heard about.

"You say it pays four bucks for every three?" he asked.

"Yep," I replied.

"And can't lose? It *automatically* wins? Must be illegal!"

"Not a bit," I replied. "In fact, the government very much approves. . ."

"Our government approves of a horse who can't lose. . ."

"Who said anything about a horse?" I asked.

"So what else could it be but a horse. . .?"

"It not only could be—but is—U. S. Savings Bonds," was my prompt reply. "The surest thing running on any track today.

"For every three dollars you invest in U. S. Savings Bonds you get four dollars back after only ten years. And if you're a member of the Payroll Savings Plan—which means you buy bonds *automatically* from your paycheck—that can amount to an awful lot of money when you're not looking. Hey, what are you doing?"

"Tearing up my racing form! The horse I'm betting on from now on is U. S. Savings Bonds."

Automatic saving is <u>sure</u> saving—U.S. Savings Bonds

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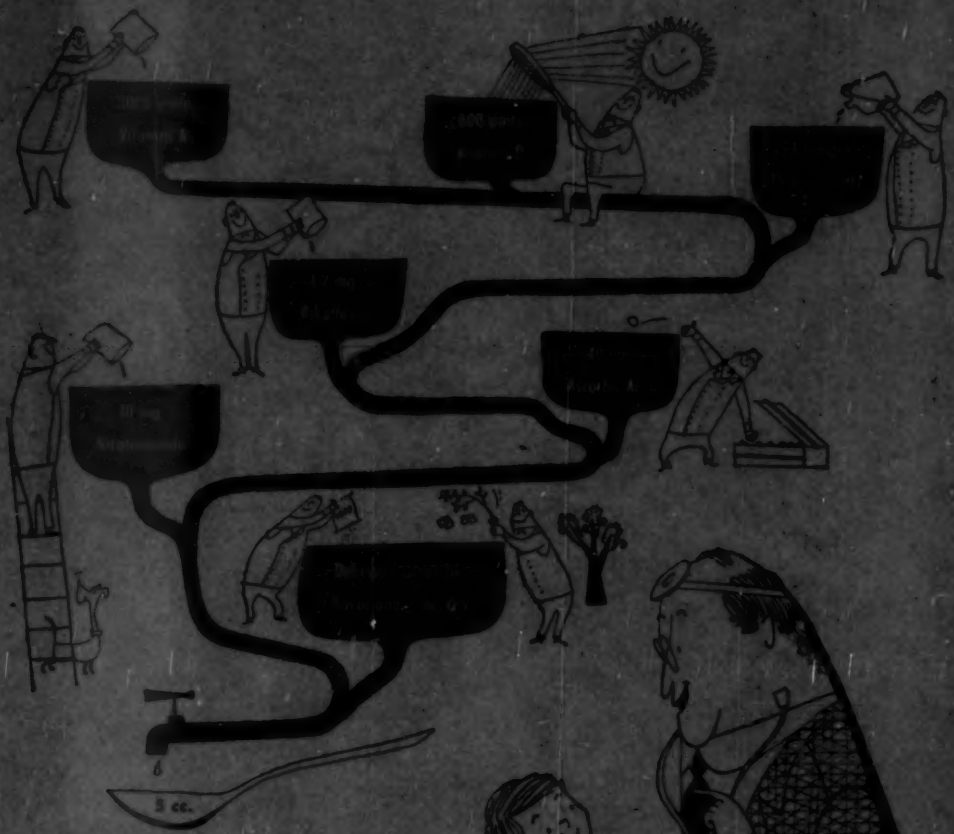

For your little patients

VI-DAYLIN

TRADE MARK

(Homogenized Mixture of Vitamins
A, D, B_1, B_2, C and Nicotinamide, Abbott)